I. AMENDMENTS

In the specification:

On page 2, please replace the paragraph beginning on line 7 with the following:

-- This application is a continuation of United States Serial Number 09/229,037, filed January 12, 1999, from which priority is claimed pursuant to 35 U.S.C. § 120, and which application is incorporated herein by reference in its entirety.--

On page 21, please replace the paragraph beginning on line 10 with the following:

--The ZFPs of the invention are engineered to recognize a selectable target site in the endogenous gene of choice. Typically, a backbone from any suitable C_2H_2 ZFP, such as SP-1, SP-1C, or ZIF268 is used as the scaffold for the engineered ZFP (*see, e.g.,* Jacobs *EMBO J.* 11:4507 (1992); Desjarlais & Berg, *PNAS* 90:2256-2260 (1993)). A number of methods can then be used to design and select a ZFP with high affinity for its target (e.g., preferably with a K_d of less than about 25 nM). As described above, a ZFP can be designed or selected to bind to any suitable target site in the target endogenous gene, with high affinity. Co-owned WO 00/42219, incorporated by reference herein in its entirety, comprehensively describes methods for design, construction, and expression of ZFPs for selected target sites.--

On page 21, please replace the paragraph beginning on line 32 with the following:

--In a preferred embodiment, co-owned WO 00/42219 provides methods that select a target gene, and identify a target site within the gene containing one to six (or more) D-able sites (see definition below). Using these methods, a ZFP can then be synthesized that binds to the preselected site. These methods of target site selection are premised, in part, on the recognition that the presence of one or more D-able sites in a target segment confers the potential for higher binding affinity in a ZFP selected or designed to bind to that site relative to ZFPs that bind to target segments lacking D-able sites. Experimental evidence supporting this insight is provided

in Examples 2-9 of co-owned WO 00/42219.--

On page 22, please replace the paragraph beginning on line 9 with the following:

--A D-able site or subsite is a region of a target site that allows an appropriately designed single zinc finger to bind to four bases rather than three of the target site. Such a zinc finger binds to a triplet of bases on one strand of a double-stranded target segment (target strand) and a fourth base on the other strand (*see* Figure 2 of co-owned WO 00/42219). Binding of a single zinc finger to a four base target segment imposes constraints both on the sequence of the target strand and on the amino acid sequence of the zinc finger. The target site with the target strand should include the "D-able" site motif 5' NNGK 3', in which N and K are convention IUPAC-IUB ambiguity codes. A zinc finger for binding to such a site should include an arginine residue at position -1 and an aspartic acid, (or less preferably a glutamic acid) at position +2. The arginine residues at position -1 interacts with the G residue in the D-able site. The aspartic acid (or glutamic acid) residue at position +2 of the zinc finger interacts with the opposite strand base complementary tot he K base in the D-able site. It is the interaction between aspartic acid (symbol D) and the opposite strand base (fourth base) that confers the name D-able site. AS is apparent from the D-able site formula, there are two subtypes of D-able sites; 5' NNGG 3' and 5' NNGT 3'. For the former site, the aspartic acid or glutamic acid at position +2 of a zinc finger interacts with a C in the opposite strand to the D-able site. In the latter site, the aspartic acid or glutamic acid at position +2 of a zinc finger interacts with an A in the opposite strand of the D-able site. In general, NNGG is preferred over NNGT.--

On page 27, please replace the paragraph beginning on line 8 with the following:

-- The biochemical properties of the purified proteins, e.g., K_d, can be characterized by any suitable assay. In one embodiment, K_d is characterized via electrophoretic mobility shift assays ("EMSA") (Buratowski & Chodosh, *in Current Protocols in Molecular Biology* pp. 12.2.1.-12.2.7 (Ausubel ed., 1996); *see also* U.S. Patent No. 5,789,538; co-owned WO 00/42219